

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 30 July 2001 (30.07.01)	
International application No. PCT/US00/21574	Applicant's or agent's file reference 3828-4000PC
International filing date (day/month/year) 08 August 2000 (08.08.00)	Priority date (day/month/year) 13 August 1999 (13.08.99)
Applicant GELBER, Cohava	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 09 March 2001 (09.03.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Maria Kirchner Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

SERUNIAN, Leslie, A.
Morgan & Finnegan, L.L.P.
345 Park Avenue
New York, NY 10154
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

18 décembre 2001 (18.12.01)

Applicant's or agent's file reference

3828-4000PC

IMPORTANT NOTIFICATION

International application No.

PCT/US00/21574

International filing date (day/month/year)

08 août 2000 (08.08.00)

1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address

VACOLD, L.L.C.
21st Floor
360 Lexington Avenue
New York, NY 10017
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☒ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address

MOLECULAR DISCOVERIES, L.L.C.
21st Floor
360 Lexington Avenue
New York, NY 10017
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to

☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☐ the International Preliminary Examining Authority ☐ otherThe International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Yukari NAKAMURA

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

3828-4000 PC
Serunian

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

To: SERUNIAN, Leslie A. et al. Morgan & Finnegan, L.L.P. 345 Park Avenue New York, New York 10154-0053 ETATS-UNIS D'AMERIQUE		Date of mailing (day/month/year) 12.11.2001
Applicant's or agent's file reference 3828-4000PC ✓		IMPORTANT NOTIFICATION
International application No. PCT/US00/21574 ✓	International filing date (day/month/year) 08/08/2000 ✓	Priority date (day/month/year) 13/08/1999 ✓
Applicant VACOLD, L.L.C. et al.		


1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide

Name and mailing address of the IPEA:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Sülberg, A Tel. +49 89 2399-7548
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PATENT COOPERATION TREATY

3828-4000 PC
SerunianFrom the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

SERUNIAN, Leslie A. et al.
Morgan & Finnegan, L.L.P.
345 Park Avenue
New York, New York 10154-0053
ETATS-UNIS D'AMERIQUE

NOTIFICATION OF RECEIPT
OF DEMAND BY COMPETENT INTERNATIONAL
PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence
and Administrative Instructions, Section 601(a))

Date of mailing
(day, month, year)

27.03.01

Applicant's or agent's file reference
3828-4000PC

IMPORTANT NOTIFICATION

International application No.

PCT/US 00/ 21574

International filing date (day, month, year)

08/08/2000

Priority date (day/month/year)

13/08/1999

Applicant

VACOLD, L.L.C. et al.

1. The applicant is hereby **notified** that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

09/03/2001

2. This date of receipt is:



the actual date of receipt of the demand by this Authority (Rule 61.1(b)).



the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).



the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. ☐ **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.



(If applicable) This notification confirms the information given by telephone, facsimile transmission or in person on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA:



European Patent Office
D-80298 Munich
Tel. (+49-89) 2399-0, Tx: 523656 epmu d
Fax: (+49-89) 2399-4465

Authorized officer

VON KEMPIS B G M

Tel. (+49-89) 2399-8577



PATENT COOPERATION TREATY

3828-4000PC

L. Serunian

From the INTERNATIONAL BUREAU

PCT

INFORMATION CONCERNING ELECTED
OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

To:

SERUNIAN, Leslie, A.
Morgan & Finnegan, L.L.P.
345 Park Avenue
New York, NY 10154
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

30 July 2001 (30.07.01)

Applicant's or agent's file reference

3828-4000PC ✓

IMPORTANT INFORMATION

International application No.

PCT/US00/21574 ✓

International filing date (day/month/year)

08 August 2000 (08.08.00) ✓

Priority date (day/month/year)

13 August 1999 (13.08.99) ✓

Applicant

VACOLD, L.L.C. et al

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

EP : AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

National : AU, BG, CA, CN, CZ, DE, IL, JP, KP, KR, MN, NO, NZ, PL, RO, RU, SE, SK, US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

AP : GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW

EA : AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

OA : BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

National : AE, AG, AL, AM, AT, AZ, BA, BB, BR, BY, BZ, CH, CR, CU, DK, DM, DZ, EE, ES, FI, GB,
GD, GE, GH, GM, HR, HU, ID, IN, IS, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MW,
MX, MZ, PT, SD, SG, SI, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

3. The applicant is reminded that he must enter the "national phase" **before the expiration of 30 months from the priority date** before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed **until 31 months from the priority date** for all States designated for the purposes of obtaining a European patent. → March 13, 2002

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer:

Maria Kirchner

Telephone No. (41-22) 338.83.38

M Kirchner

PATENT COOPERATION TREATY

3828-4000PC

RECEIVED

Serunian

From the INTERNATIONAL BUREAU

PCT

**NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT**

(PCT Administrative Instructions, Section 411)

To:

2000 DEC 19 P 1:02

SERUNIAN, Leslie, A. & FINNEGAN LLP
Morgan & Finnegan, L.L.P.
345 Park Avenue
New York, NY 10154
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 11 December 2000 (11.12.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 3828-4000PC	
International application No. PCT/US00/21574	
International filing date (day/month/year) 08 August 2000 (08.08.00)	
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 13 August 1999 (13.08.99)
Applicant VACOLD, L.L.C. et al	

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
13 Augu 1999 (13.08.99)	09/374,367	US	27 Sept 2000 (27.09.00)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

S. Mandallaz

Telephone No. (41-22) 338.83.38

PATENT COOPERATION TREATY

3828-4000 PC
LAS.

RECEIVED

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF RECEIPT OF
RECORD COPY

(PCT Rule 24.2(a))

To:

2000 OCT 11 P 2:20

SERUNIAN, Leslie, A. & FINNEGAN LLP
Morgan & Finnegan, L.L.P.
345 Park Avenue
New York, NY 10154
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 22 September 2000 (22.09.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 3828-4000PC ✓	International application No. PCT/US00/21574 ✓

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

VACOLD, L.L.C. (for all designated States except US)

GELBER, Cohava (for US)

International filing date : 08 August 2000 (08.08.00) ✓
 Priority date(s) claimed : 13 August 1999 (13.08.99) ✓
 Date of receipt of the record copy by the International Bureau : 01 September 2000 (01.09.00)
 List of designated Offices :

AP : GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW
 EA : AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 EP : AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 OA : BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 National : AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

- ☒ time limits for entry into the national phase
☐ confirmation of precautionary designations
☒ requirements regarding priority documents

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. (41-22) 740.14.35</p>	<p>Authorized officer: Y. KUWAHARA</p> <p>Telephone No. (41-22) 338.83.38</p>
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INFORMATION ON TIME LIMITS FOR ENTERING THE NATIONAL PHASE

The applicant is reminded that the "national phase" must be entered before each of the designated Offices indicated in the Notification of Receipt of Record Copy (Form PCT/IB/301) by paying national fees and furnishing translations, as prescribed by the applicable national laws.

The time limit for performing these procedural acts is **20 MONTHS** from the priority date or, for those designated States which the applicant elects in a demand for international preliminary examination or in a later election, **30 MONTHS** from the priority date, provided that the election is made before the expiration of 19 months from the priority date. Some designated (or elected) Offices have fixed time limits which expire even later than 20 or 30 months from the priority date. In other Offices an extension of time or grace period, in some cases upon payment of an additional fee, is available.

In addition to these procedural acts, the applicant may also have to comply with other special requirements applicable in certain Offices. **It is the applicant's responsibility** to ensure that the necessary steps to enter the national phase are taken in a timely fashion. Most designated Offices do not issue reminders to applicants in connection with the entry into the national phase.

For detailed information about the procedural acts to be performed to enter the national phase before each designated Office, the applicable time limits and possible extensions of time or grace periods, and any other requirements, see the relevant Chapters of Volume II of the PCT Applicant's Guide. Information about the requirements for filing a demand for international preliminary examination is set out in Chapter IX of Volume I of the PCT Applicant's Guide.

GR and ES became bound by PCT Chapter II on 7 September 1996 and 6 September 1997, respectively, and may, therefore, be elected in a demand or a later election filed on or after 7 September 1996 and 6 September 1997, respectively, regardless of the filing date of the international application. (See second paragraph above.)

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

CONFIRMATION OF PRECAUTIONARY DESIGNATIONS

This notification lists only specific designations made under Rule 4.9(a) in the request. It is important to check that these designations are correct. Errors in designations can be corrected where precautionary designations have been made under Rule 4.9(b). The applicant is hereby reminded that any precautionary designations may be confirmed according to Rule 4.9(c) before the expiration of 15 months from the priority date. If it is not confirmed, it will automatically be regarded as withdrawn by the applicant. There will be no reminder and no invitation. Confirmation of a designation consists of the filing of a notice specifying the designated State concerned (with an indication of the kind of protection or treatment desired) and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.

REQUIREMENTS REGARDING PRIORITY DOCUMENTS

For applicants who have not yet complied with the requirements regarding priority documents, the following is recalled.

Where the priority of an earlier national, regional or international application is claimed, the applicant must submit a copy of the said earlier application, certified by the authority with which it was filed ("the priority document") to the receiving Office (which will transmit it to the International Bureau) or directly to the International Bureau, before the expiration of 16 months from the priority date, provided that any such priority document may still be submitted to the International Bureau before that date of international publication of the international application, in which case that document will be considered to have been received by the International Bureau on the last day of the 16-month time limit (Rule 17.1(a)).

Where the priority document is issued by the receiving Office, the applicant may, instead of submitting the priority document, request the receiving Office to prepare and transmit the priority document to the International Bureau. Such request must be made before the expiration of the 16-month time limit and may be subjected by the receiving Office to the payment of a fee (Rule 17.1(b)).

If the priority document concerned is not submitted to the International Bureau or if the request to the receiving Office to prepare and transmit the priority document has not been made (and the corresponding fee, if any, paid) within the applicable time limit indicated under the preceding paragraphs, any designated State may disregard the priority claim, provided that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity to furnish the priority document within a time limit which is reasonable under the circumstances.

Where several priorities are claimed, the priority date to be considered for the purposes of computing the 16-month time limit is the filing date of the earliest application whose priority is claimed.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 3828-4000PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 21574	International filing date (day/month/year) 08/08/2000	(Earliest) Priority Date (day/month/year) 13/08/1999
Applicant VACOLD, LLC		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

6

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

National Application No.

PCT/US 00/21574

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/30 C12N5/06 C07K14/47 G01N33/53 B01D15/08
 A61K39/395 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 88 03954 A (CENTOCOR INC) 2 June 1988 (1988-06-02) page 1, line 1 -page 4, line 22 page 20, line 19 -page 35, line 4; claims 1-22 ---	2,7,16, 20-23, 25,35, 37,40
A	WO 96 26964 A (PROTEIN DESIGN LABS INC ;IOWA IMMUNOTHERAPY INVESTIGATO (US)) 6 September 1996 (1996-09-06) page 11, line 26 -page 27, line 21 ---	1,6,8,9, 11,18, 20-23, 35,39,42
A	WO 94 05329 A (JENNER TECHNOLOGIES) 17 March 1994 (1994-03-17) page 3, line 23 -page 11, line 29 --- -/--	10



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *F* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

16 January 2001

Date of mailing of the international search report

23/01/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5518 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel (+31-70) 340 2040, Tx 31 651 epo nl,
 Fax (+31-70) 340 3016

Authorized officer

Mateo Rosell, A.M.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/21574

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 96 40295 A (KOSTAKOGLU LALE ;DIVGI CHAITANYA R (US); SLOAN KETTERING INST CANC) 19 December 1996 (1996-12-19)</p> <p>page 12, paragraph 2 -page 18, paragraph 1 page 69-78 page 89-123</p> <p>---</p>	<p>2,7,16, 20-24, 35-38, 40,42-44</p>
A	<p>PARTINGTON K M ET AL: "A novel method of cell separation based on dual parameter immunomagnetic cell selection" JOURNAL OF IMMUNOLOGICAL METHODS,NL,ELSEVIER SCIENCE PUBLISHERS B.V.,AMSTERDAM, vol. 223, no. 2, 4 March 1999 (1999-03-04), pages 195-205, XP004158718 ISSN: 0022-1759 abstract page 195, left-hand column, paragraph 1 -page 196, left-hand column, paragraph 3 page 204, right-hand column, paragraph 2 -page 205, left-hand column, paragraph 1</p> <p>---</p>	<p>18</p>
A	<p>OZAKI S ET AL: "IMMUNOTHERAPY OF MULTIPLE MYELOMA WITH A MONOCLONAL ANTIBODY DIRECTED AGAINST A PLASMA CELL-SPECIFIC ANTIGEN, HM1.24" BLOOD,W.B. SAUNDERS, PHILADELPHIA, VA,US, vol. 90, no. 8, 15 October 1997 (1997-10-15), pages 3179-3186, XP002918597 ISSN: 0006-4971 the whole document</p> <p>---</p>	<p>2,7,16, 20-23, 35,37,40</p>
P,A	<p>TAI Y -T ET AL: "Isolation and characterization of human multiple myeloma cell enriched populations" JOURNAL OF IMMUNOLOGICAL METHODS,NL,ELSEVIER SCIENCE PUBLISHERS B.V.,AMSTERDAM, vol. 235, no. 1-2, February 2000 (2000-02), pages 11-19, XP004188227 ISSN: 0022-1759 the whole document</p> <p>-----</p>	<p>1,14,25, 26</p>

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/21574

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
W0 8803954	A	02-06-1988	US 5059680 A	22-10-1991
			AT 97448 T	15-12-1993
			CA 1305416 A	21-07-1992
			DE 3788229 D	23-12-1993
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PATENT COOPERATION TREATY

PCT

REC'D 14 NOV 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3828-4000PC		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/21574	International filing date (day/month/year) 08/08/2000	Priority date (day/month/year) 13/08/1999	
International Patent Classification (IPC) or national classification and IPC C07K16/30			
Applicant VACOLD, L.L.C. et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 09/03/2001	Date of completion of this report 12.11.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer BROCHADO GARGANTA, M Telephone No. +49 89 2399 8935 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/21574

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-45 as originally filed

Claims, No.:

1-44 as originally filed

Drawings, sheets:

1/10-10/10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

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☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-44
	No: Claims
Inventive step (IS)	Yes: Claims 1-44
	No: Claims
Industrial applicability (IA)	Yes: Claims 1-44
	No: Claims

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

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Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

(A) WO 88 03954 A

2. The intermediate document cited in the Search Report (*Tai Y -T et al: 'Isolation and characterization of human multiple myeloma cell enriched populations' Journal of Immunological Methods, vol. 235, no. 1-2, February 2000 (2000-02), pages 11-19*) could be considered as state of the art, if the date of priority is not validly claimed for the relevant parts of the present application.

3. Novelty

Claim 1, relating to a monoclonal antibody or binding fragment thereof, is new in the sense of Article 33(2) PCT, because an antibody which binds to an antigen on the surface of a human myeloma cell, wherein said antigen has a molecular weight of 78 kDa to 120 kDa and is absent from human peripheral blood mononuclear cells, human B cells and human B cell myelogenic leukemia cells, is not disclosed in the prior art.

The same applies to claims 2-44. Thus, these claims are considered to be novel (Article 33(2) PCT).

4. Inventive step

- 4.1 Claim 1 relates to a monoclonal antibody or binding fragment thereof, which specifically binds to an antigen on the surface of a human myeloma cell, wherein said antigen is glycosylated and has a molecular weight of 78 kDa to 120 kDa. Moreover, this antigen is absent from peripheral blood mononuclear cells, absent from human B cells and absent from human B cell myelogenic.

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The monoclonal antibody of the present application (VAC69), produced by the hybridoma deposited under ATCC Accession No. PTA-450, was shown to react with a single chain cell surface glycoprotein with a Mr of 78-120 kDa. The **VAC69 did not react with an array of human cancers such as lung, prostate, breast, cervical, neuroblastoma, lymphoma and leukemia. Moreover, the antigen was not detected in human normal tissues such as those derived from breast, ovary, prostate, colon or lung.**

There is no reference in the prior art to such an antibody.

Document A discloses an antibody against an isolated antigen (CA 125), which is a tumor-associated antigen expressed on ovarian epithelial tumors, having a molecular weight of about 200 kDa and being glycosylated (see claims 1, 2 and 22; pages 1 and 32). This antigen is present in various sources, like for example, human serum, human milk, normal cervical mucous, central airway and normal lung tissue (see page 1 and page 34).

The difference between the subject-matter of claim 1 and the disclosure in document A is the fact that the claimed antibody does not react with an array of human cancers and that its antigen is not present in normal tissues and has a different molecular weight.

The antibody of the present application only shows a reaction with myeloma, ovarian cancer and liver cancer cells. It recognises a communal epitope of (at least) two antigens, i.e. one of a Mr of 78-120 kDa (myeloma cells) and one of 76-213 kDa (ovarian cancer cells).

The binding of this antibody to cancer cells causes growth inhibition or killing of said tumor cells. Therefore, this antibody is very useful for establishing a method for removing these specific cancer cells. The antibody of document A does not show specificity for a cancer type, being not only present in several cancer cells but also in normal tissue. That means that this antibody is not able of destroying selectively the cancer cells, which should be inhibited, but would also destroy normal cells having the antigen capable of reacting with the antibody.

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Thus, claim 1 is considered to be based on an inventive concept as required by Article 33(3) PCT.

- 4.2 Claims 2-44 relate to the antibody, to antigens which would be recognised by said antibody, to the use of said antibody in the manufacture of a medicament to localise or inhibit myeloma or ovarian cancer cells, a myeloma producing this antibody, a method for detecting said cells, and a pharmaceutical composition comprising the antibody.

For the reasons given in 4.1, these claims are also considered to be based on an inventive concept as required by Article 33(3) PCT.

Re Item VIII

Certain observations on the international application

1. Claim 1 relates to a monoclonal antibody, characterised by property features of the antigen against it will react. It is not possible for the skilled person with basis on these characteristics, to arrive to the claimed antibody. The hybridoma cell line producing this antibody has however been deposited at the American Type Culture Collection having the ATCC Accession No. PTA-450 (see for example claim 4 of the present application). This feature (claim 4) should be referred to in claim 1, for rendering the claim clear (Article 6 PCT). The same applies to the features of claims 13, 17 and 19, which should belong to claims 11, 16 and 18, respectively.
2. The wording "further characterised in that" (see claims 1 and 11) renders the claims unclear (Article 6 PCT), as it is not clear which features are already characterising the antibody.

Moreover, the wording "specifically binds" (see for example claim 1) seems to be not correctly used, as the antibody is capable of binding an epitope on the surface of human myeloma cells, as well as one on the surface of ovarian cancer cells.

3. An essential feature of the claimed monoclonal antibodies is the fact that they are specific for binding an antigen on the surface of human myeloma cells and another

antigen on the surface of ovarian cancer cells. That means that this antibody will not bind to other epitopes on other cancer or normal cells. Therefore, claim 3 is redundant and could implicitly mean that the antibody of claim 1 would be capable of binding to such cells. Thus, claim 3 should be deleted.